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Hematopoietic Neoplasms of Slaughter Animals^{1, 2}

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HEMATOPOIETIC NEOPLASMS observed in cattle, pigs, sheep, goats, and horses slaughtered in federally inspected establishments of the United States are: a) *malignant lymphomas*; b) *thymomas*; c) *mastocytomas*; and d) *granulocytic sarcomas* (malignant myelomas).

Malignant lymphomas are the most frequently observed hematopoietic neoplasms of animals of all 5 species (tables 1 and 2). Rates in individual species cannot be compared to each other because of a lack of uniform information about such characteristics of slaughter animals as age, condition, and their care. Except for minor variations in distributions of neoplastic infiltrates, morphologic patterns are similar in all 5 species and resemble those seen in lymphomas of other animals and man.

TABLE 1.—Rates of occurrence of malignant lymphomas per 100,000 animals presented for slaughter, July 1957–June 1967

Fiscal year	Cattle	Calves	Sheep	Goats	Pigs	Horses and mules
1958	17.63	1.76	0.37	0	1.32	0
1959	18.19	1.91	.61	0	1.53	1.14
1960	16.92	2.63	.68	3.28	1.44	10.45
1961	18.86	2.11	.52	2.34	1.70	2.02
1962	18.79	2.13	.48	0	1.90	0
1963	17.06	1.85	.39	0	2.07	10.57
1964	17.01	3.10	.41	1.15	1.84	0
1965	17.91	2.35	.31	0.77	1.98	2.89
1966	17.89	2.25	.38	0.57	1.99	18.75
1967	17.51	2.36	.55	0.99	1.92	16.54

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TABLE 2.—Histopathologically confirmed hematopoietic neoplasms submitted by veterinary meat inspectors, July 1957–June 1967

Neoplasm	Cattle	Calves	Sheep	Goats	Pigs	Horses and mules
Malignant lymphomas	900	9	17	2	200	3
Chronic granulomatous disease	—	—	—	—	35	—
Thymomas	29	—	2	12	5	2
Mastocytomas	12	—	—	—	5	—
Granulocytic sarcomas	2	—	—	—	2	—
Plasma cell neoplasms	—	—	—	—	—	—

Thymomas occur in animals of all 5 species (table 2). They are encapsulated thoracic masses—composed of mixtures of reticular and lymphocytic cells—characteristically benign and rarely metastatic. Goats appear to have a relatively high incidence of thymomas compared to animals of the other 4 species.

Mastocytomas, rare in slaughter animals were found only in cattle and pigs (table 2).

Granulocytic sarcomas (malignant myelomas), also rare in slaughter animals, were observed only in cattle and pigs (table 2). Distribution of infiltrates was characteristic of granulocytic sarcoma rather than of leukemia. The outstanding characteristic was the green color of gross organs.

MATERIALS

Material from more than 18,000 animals was histopathologically examined in the Pathology Laboratory of the Federal Meat Inspection Service of the U.S. Department of Agriculture during the 10-year period 1957–67. Descriptions of hematopoietic neoplasms in this report are based on examination of material submitted by veterinary meat inspectors (table 2). In federally inspected slaughterhouses, antemortem and postmortem examinations of all animals are performed by uniform systematic procedures (1). If a veterinary meat inspector detects clinical signs and/or lesions at necropsy that are unusual or atypical or that require histopathologic confirmation, he submits representative material and a written description of gross observations to the Pathology Laboratory.

Calves are defined as cattle younger than 1 year. Cattle, pigs, and sheep can be divided into two groups with potentially important implications in the epizootiology of neoplasms and comparative oncology. One group, *feeders*, are young, sexually mature animals (cattle 1–3 years of age, pigs 6–8 months, and sheep under 1 year) that have been confined in feedlots for feeding of concentrated fattening rations for a specific number of days before slaughter. The other group, *adults*, are older animals kept for vary-

ing lengths of time for breeding and other commercial purposes and sent to slaughter when they become unproductive. Approximately 80% of cattle, 92% of pigs, and 93% of sheep slaughtered under federal meat inspection specifications are feeders and the remainder are adults. Most goats and horses are adults when slaughtered.

Occurrence rates of hematopoietic neoplasms other than malignant lymphomas cannot be determined accurately because veterinary meat inspectors submit material for histopathologic confirmation only when gross lesions are unusual or questionable. Obvious neoplasms are not always submitted for confirmation. The laboratory receives disproportionately high numbers of relatively unusual tumors.

Because submitted specimens may be limited to material from primary sites, extent of disease cannot always be determined. Descriptions based on postmortem examinations are often limited to the most extensive lesions. Information about involvement of other structures is often minimal. In contrast to animals included in epizootiologic surveys or hospital clinic populations, most animals slaughtered for food are young, just sexually mature, and in a well-nourished state. These factors must be considered when data on distribution and characterization of neoplasms observed in slaughtered animals are compared to those from sources in which diseases are permitted to run their course.

Studies of material from animals condemned in slaughterhouses offer opportunities to collect material from relatively large populations of animals. They have their disadvantages in that complete clinical and epidemiological information is usually not available.

Numbers of animals slaughtered in the United States each year in establishments under federal jurisdiction are recorded in table 3 (2-5). These figures represent approximately 80% of the animals slaughtered in the United States.

TABLE 3.—Numbers of animals slaughtered in U.S. federally inspected establishments, July 1957-June 1967

Fiscal year	Millions					
	Species					
	Cattle	Calves	Sheep	Goats	Pigs	Horses and mules
1958	18.58	6.65	12.88	0.17	59.20	0.13
1959	17.32	5.14	12.80	.19	63.87	.09
1960	18.46	4.98	13.45	.06	70.50	.07
1961	19.86	5.20	14.92	.09	64.21	.05
1962	20.16	5.01	14.67	.10	67.11	.05
1963	20.86	4.77	14.14	.26	69.31	.05
1964	23.20	4.54	13.70	.17	72.16	.04
1965	25.81	5.02	12.32	.26	68.54	.03
1966	27.38	4.92	11.65	.35	60.66	.04
1967	27.87	4.19	11.63	.50	68.68	.04

All material submitted to the laboratory by veterinary meat inspectors is fixed in 10% buffered formalin. Except for occasional use of special stains such as Giemsa, Wilder's reticulum, and toluidine blue, paraffin-embedded sections are stained routinely with hematoxylin and eosin.

MALIGNANT LYMPHOMAS

Malignant lymphomas are also called lymphosarcoma, leukosis, lymphoblastoma, lymphadenosis, lymphomatosis, lymphocytoma, aleukemic leukemia, and pseudoleukemia.

Surveys of neoplasms of farm animals from several countries of the world indicate that lymphomas are among the most prevalent neoplasms of large domestic animals (6-13). Such surveys indicate not only relative frequencies of neoplasms of different cell types in a single species but also provide some information concerning relative frequencies of specific neoplasms in more than one species.

A review of malignant lymphomas in domesticated mammals has been provided by Jarrett *et al.* (14) who described etiologic and epidemiologic studies in Europe and in the United States. The review by Smith (8) summarized knowledge of malignant lymphomas in animals, particularly cattle. Bendixen's report (16) of bovine malignant lymphomas (leukosis) in Denmark illustrates the complexity of this disease in its various manifestations. Several investigators (17-21) have reported epizootologic studies of bovine malignant lymphomas in specific geographic areas of the United States. We are not aware of similar studies of malignant lymphomas in slaughter animals other than cattle.

The only statistics on incidence of malignant lymphomas of large domestic animals other than cattle in the United States are those of the Federal Meat Inspection Service (2-4) (table 1). Actual rates are probably higher than those recorded because these statistics do not include animals that died on farms or that were slaughtered in establishments not under the jurisdiction of federal meat inspectors.

During a 10-year period (July 1957 through June 1967), rates of malignant lymphomas of cattle, pigs, and sheep remained relatively constant (table 1). Average rates, expressed as numbers of lymphomas observed per 100,000 slaughtered animals per year, were: cattle, 18/100,000; calves, 2/100,000; pigs, 2/100,000; and sheep, 0.5/100,000. The apparent differences in annual rates of lymphomas of goats, horses, and mules reflect variations in numbers, ages, and conditions of animals slaughtered in a given year and cannot be interpreted as actual differences in incidences.

Gross Descriptions

Malignant lymphomas are usually white to grayish-white, fleshy masses with little or no lobulation. Color depends on the amounts of necrosis,

hemorrhage, and congestion. Malignant lymphomas may be nodular or diffuse. Consistency depends on amounts of supporting connective tissue. Malignant lymphomas involve many organs and tissue structures, as described by Smith (22) in his study of malignant lymphoma in 1,000 slaughtered cattle.

Classification of Malignant Lymphomas

The term *malignant lymphoma*, defined by Gall and Mallory (23) and later by Gall and Rappaport (24), has been used by the U.S. Federal Meat Inspection Service since 1953 (25) to designate various forms of lymphoid neoplasms.

Malignant lymphomas observed in slaughter animals can be classified into four major types. An additional category designated *granulomatous* includes those rare animal neoplasms which resemble Hodgkin's disease of man. Cell types vary morphologically; the various categories overlap.

a) The *lymphocytic type* is characterized by cells that are uniform in size and shape. Staining density varies little. Component cells are slightly larger than normal lymphocytes. Nuclei are round and chromatin granules tend to be concentrated near nuclear membranes. Cytoplasm is scant (fig. 1).

b) The *lymphoblastic type* is composed of cells slightly larger than those of the lymphocytic type. The cells are of about the same size and shape. Nuclei are large and round. Abundant chromatin granules, evenly distributed within the nuclei, look like hyperchromasia. Some nuclei may be indented. Cytoplasm is more abundant than in cells of the *lymphocytic type*, and cytoplasmic boundaries are distinct.

c) The *histiocytic type* is characterized by cellular pleomorphism. Variations in cells in a single field are more obvious at high magnifications. Component cells are larger and vary more in size and shape than those of the *lymphoblastic type*. Most nuclei are oval and may be indented or kidney-shaped. Pale eosinophilic cytoplasm is abundant and cytoplasmic processes may extend in various directions (figs. 2 and 3). Bengston (26) in 1938 first reported a *reticulum cell sarcoma* in a cow. He used silver stains to demonstrate the "reticular" nature of histiocytes or "reticulum cells." Small, spherical "punched-out" areas ("starry sky") are sometimes observed in the histiocytic type, particularly near necrotic areas (fig. 4).

d) The *mixed types* are malignant lymphomas composed of cells of two or more cell types.

e) The *granulomatous type* is characterized by fibrosis and proliferation of histiocytes and polymorphonuclear eosinophils. Occasional multinucleated giant cells may be observed. Hemorrhage and congestion of involved organs are prominent. The *chronic granulomatous disease* of pigs, described by Forbus and Davis (27), is included in this category. Similar processes have not been described in other slaughter animals except for a report by

Runnells and Benbrook (28) who described a malignant lymphoma of a horse in which microscopic lesions resembled those of Hodgkin's disease.

As in man, reactive hyperplasias of animal lymph nodes are often difficult to distinguish from neoplastic processes. Criteria for distinguishing reactive and neoplastic changes in lymph nodes have been described by Rappaport (29). Because regional lymph nodes are included in most routine specimens received in our laboratory, regardless of the primary disease, we have had many opportunities to observe the various histomorphologic changes occurring in nodes which drain sites subjected to a variety of insults; changes in many of these nodes are proliferative and may mimic lymphomas. The problem is less difficult when there is complete obliteration of nodal architecture by a lymphomatous process or when a neoplasm can be demonstrated in other organs or tissues of the body.

Malignant Lymphomas of Cattle

Of material submitted to the Pathology Laboratory by veterinary meat inspectors during 1957-67, diagnoses of malignant lymphoma were confirmed by histologic examination in 900 cattle and 9 calves (table 2). Malignant lymphoid neoplasms in very young cattle have been reported by Hatzioles (30), who described a malignant lymphoma in a bovine fetus, and by Misdorp (31), who observed lymphatic leukoses in 2 newborn calves. Eighty-five percent of cattle of our series in which diagnoses of lymphomas were made were 3 years old or more. Approximately 20% showed evidence of poor health at slaughter, although no definite correlations could be made between cell types of lymphomas and effects on general health of animals. Clinical signs and courses of disease would of course depend on anatomic sites of involvement, duration, and extent of disease. Clinical features of 59 bovine lymphomas in which the disease was allowed to run its course have been described by Marshak *et al.* (17).

Lymph nodes were involved in most bovine lymphomas of our series. Evaluations of enlarged lymph nodes of cattle, like those of other animals, depend on several factors and details of clinical histories, and postmortem examinations must be considered in addition to the histologic appearance of the node. Because lymph nodes of calves normally contain active lymphoid tissue, special care must be taken when the nodes are evaluated. Lymphomatous lymph nodes from cattle may be enlarged as much as 4-6 times. They are whitish gray and friable. Petechiae and focal areas of necrosis may be observed.

The heart was involved in more than 50% of cattle (fig. 5). The malignant process is believed to begin in the right auricle. The neoplastic cells characteristically infiltrate the myocardium, gradually replacing the muscle fibers (fig. 6). Jarplid (32) explained the high incidence of right auricular involvement in cattle on the basis that subepicardial tissue remains undifferentiated and responds readily to proliferative stimuli.

The stroma of the myocardium and heart valves are apparently the last structures to be destroyed by the malignant process, since hydrothorax and passive congestion of the liver were rare in these animals.

Spleens were affected in approximately 19% of cattle. They were enlarged as much as 3-5 times. The cut surface was maroon and of semi-solid consistency, in contrast to the bright-red and bloody appearance of a congested spleen.

Hemal nodes, histologically and physiologically similar to the spleen, are found only in ruminants (33). They are located near the hilus of lymph nodes in various organs and in subcutaneous adipose tissue—especially on the back and in other sites. Hemal nodes may be involved in lymphomas. Because they are easily accessible for biopsy, some investigators have suggested biopsy of subcutaneous hemal nodes as a method for early diagnosis of malignant lymphoma (34).

Kidneys were involved in approximately 18% of cattle. The neoplasm was usually nodular and multiple. Nodules were most numerous in cortices with growth toward medullary regions (fig. 7). These infiltrates must be differentiated from those of a more common non-neoplastic inflammatory process, focal nonsuppurative embolic nephritis. In lymphomas, walls of ureters and urinary bladder may also be invaded: In these organs, neoplastic cells proliferate in lamina propria and invade other layers.

The uterus was involved in at least 10% of bovine lymphomas. This is probably a low estimate because the uterus, being an "inedible" organ, is not ordinarily examined so thoroughly as other organs. Despite widespread involvement of other organs by a malignant lymphoma, the uterus may not be examined, or if examined, may not be specifically described in necropsy reports. Lymphomas of the uterus usually appear as multiple, large, nodular masses in the wall (figs. 8 and 9). In advanced stages, the uterine wall may be diffusely thickened, up to 8 cm.

Livers were involved in approximately 10% of adult cattle and in most calves of our series. Hepatic foci were characteristically multiple, whitish-gray nodules of varying sizes distributed throughout the parenchyma. Some livers, which did not contain grossly visible nodules, were enlarged and pale, an appearance characteristic of diffuse infiltrations by neoplastic cells. Microscopically, several variations in patterns of neoplastic involvement of livers were noted. In some, neoplastic cells were arranged in discrete nodular masses. In others, the cells formed wide collars around hepatic lobules. In a few, neoplastic lymphoid cells were found only in the sinusoids (fig. 10) despite lack of evidence of leukemia in other organs. Because hematologic information was not available for slaughter animals, we could not correlate morphologic patterns with hematologic information.

The walls of the gastrointestinal tract, particularly of the abomasum (fourth or glandular compartment of stomach of ruminants), were involved in 8% of animals. A higher incidence of gastrointestinal involvement might have been anticipated because of the presence of lymphoid tissue in the walls.

Lungs were involved in 9% of animals. The infiltrates were distinct, whitish nodules which ranged from 2-4 cm in diameter. These pulmonary infiltrates probably originated in intrapulmonary lymph nodules.

In fewer than 1% of cattle, malignant lymphomas involved the vertebral canal in the region of the terminal spinal cord (fig. 11). Clinically, involvement of the spinal canal is known to paralyze hind limbs by pressure on motor nerves.

Multiple, ovoid masses of tumor measuring up to 30 cm in diameter were observed in thoracic, abdominal, and pelvic cavities of 16% of cattle. These masses of tumor probably originated in lymph nodes. Clinically, such masses in pelvic regions are known to cause paresis of hind limbs by pressure on nerve trunks.

Lymphomatous nodules of the skin were observed in fewer than 1% of animals. All animals with skin infiltrates also had involvement of lymph nodes. Marshak *et al.* (35) described in detail a generalized malignant lymphoma with cutaneous involvement in a heifer, and Carson and Jones (36) described one in an 8-year-old cow. Clegg and Moss (37) described skin leukosis in a 3-year-old heifer which died 3 years later from malignant lymphoma of the heart. Bendixen (16) believes that skin involvement indicates a distinctive type of malignant process with a pathogenesis different from that of other forms of bovine lymphoma (leukoses).

Thymic involvement was observed in lymphomas of at least 2% of cattle in our series and was always a part of a generalized process that included lymph nodes and other organs. It was frequently difficult to determine whether a mass in the anterior thorax was thymus, or included thymus. We have recorded thymic involvement only in those animals in which the organ was specifically identified at necropsy or in those in which Hassall's corpuscles or other characteristic structures were observed in histologic sections. Dungworth *et al.* (38) reported details of 14 generalized malignant lymphomas of cattle in which thymus was said to be the organ most severely affected.

True thymomas are quite different from malignant lymphomas and are described in a separate section of this report.

Exophthalmus, associated with malignant lymphoma of the orbit and retrobulbar tissues, was observed in several cattle.

We did not have an opportunity to examine bone marrow from any cattle. However, we know that bone marrow involvement occurs in significant numbers of malignant lymphomas of cattle, as described by Dungworth *et al.* (38).

The relationship between leukemia and malignant lymphoma has not been established. Weber (39) reported that only 5-10% of cattle affected by malignant lymphoma had hematologic evidence of leukemia. Herzog (40) and Thompson and Roderick (41) also reported little correlation between hematologic findings and malignant lymphoma. In Denmark, much emphasis is placed on the number of lymphocytes in the peripheral

blood, and persistent lymphocytoses in adults are considered to indicate a pretumorous stage. Those interested in this theory should consult the work of Bendixen (16).

The extent of involvement by malignant lymphoma in slaughtered cattle is difficult to determine because not all affected organs or body systems are mentioned specifically in necropsy reports. However, in most cattle the lymphomas were specifically described in more than one group of lymph nodes and/or body systems. Malignant lymphoma may occur in almost any part of the body as either a primary or a metastatic neoplasm.

Morphologic classification of bovine lymphomas of 909 cattle of our series indicated that 20% were *lymphocytic*, 38% *lymphoblastic*, 35% *histiocytic*, and 7% *mixed*. Granulomatous forms were not observed in cattle. Morphologic characteristics of cells varied in different affected nodes and organs in specific animals.

Malignant Lymphomas of Pigs

Lymphomas are observed in slaughtered pigs at an average annual rate of 2/100,000 (tables 1 and 2). Sixty percent of 200 histologically confirmed cases in our series were in pigs 6-8 months old. It must be emphasized that 92% of all pigs slaughtered are this age, and valid comparisons of rates between species cannot be made.

Twenty-five percent of affected pigs showed some clinical evidence of disease possibly related to underlying lymphomas. In more than 90% of pigs, lymphomas involved more than one body system or group of lymph nodes, although the disease did not appear to be as widespread in the body as in cattle. In several animals, lymphomas were found only in the liver (figs. 12 and 13) and/or kidney. Lungs and gastrointestinal tract were less often involved. In contrast to lymphomas of cattle, those of pigs rarely involved the heart. Infiltrates were not observed in uterus or spinal meninges.

Microscopic examination revealed that approximately 42% of porcine lymphomas were *lymphocytic*, 34% were *lymphoblastic*, 15% *histiocytic*, and 9% *mixed*. Tumor cell distributions within affected organs were similar to those of cattle.

Chronic Granulomatous Disease of Pigs

During the 10-year period, we had an opportunity to study material from 35 pigs with the chronic granulomatous disease described in 1946 by Forbus and Davis (27) (table 2). This disease is described in this paper because the original investigators believed that morphologic changes resembled those of human Hodgkin's disease.

Incidence of this granulomatous disease of unknown etiology is probably higher than our figures indicate because veterinary meat inspectors who submit material for histologic confirmation are usually not familiar with the disease.

Seventy percent of pigs with this entity were 1 year of age and older, which suggests that the disease is one of older animals, although the process may begin relatively early in life. Characteristics of the clinical course are not known because the disease had not been recognized during life; evidence of anemia and icterus was observed in some carcasses, however. The disease has never been linked to an infectious agent.

Grossly, the most striking and constant necropsy findings were the greatly enlarged and often massive and hard spleens (from 4-15 times normal size) (figs. 15 and 16), which contained many red-and-white mottled areas, and enlarged cirrhotic livers. One spleen weighed 17 pounds; the normal pig's spleen weighs $\frac{1}{2}$ to 1 pound on the average. Livers were enlarged 2-4 times and were pale because of excessive fibrosis. Thick, white interlobular connective tissue bands separated hepatic lobules. Lymph nodes, kidneys, and bone marrow were sometimes affected. Lymph nodes were enlarged and congested when involved in the malignant process.

Microscopically, much normal splenic parenchyma had been replaced by a diffuse granulomatous process. Early stages were characterized by infiltrations of histiocytes and eosinophils, congestion, and hemorrhage. Advanced stages were characterized by diffuse fibrosis and depletion of lymphoid tissue (fig. 17). The differences in degrees of cellular infiltrates and fibrosis suggest that the disease is chronic and that we observed different stages of the disease process. Multinucleated giant cells, some of which resembled megakaryocytes, were observed in spleens of some animals (fig. 18). Cells with features of Reed-Sternberg cells were not observed in animals of our series although they have been reported (27).

A diffuse granulomatous process with extensive proliferation of interlobular connective tissue was noted in livers. Small collections of polymorphonuclear eosinophils and mononuclear leukocytes were scattered in connective tissue (fig. 19). Proliferation of biliary ducts was observed in livers of some animals. Gradual encroachment on hepatic lobules resulted in atrophy or destruction of liver cells in advanced stages of the disease.

In most pigs the lymph nodes were not affected, although in nodes of some animals, a granulomatous process similar to that of the spleen was observed (fig. 20).

Forbus and Davis reported that focal granulomatous lesions similar to those of the spleen were also observed in bone marrow and kidneys.

The etiology and pathogenesis of this disease need clarification.

Malignant Lymphomas of Sheep

Malignant lymphomas of sheep occur at a rate of approximately 0.5/100,000 slaughtered animals per year. Of 17 histologically confirmed lymphomas of sheep of our series, all but 2 were in older animals (table 2). All sheep had multiple neoplasms in different parts of the carcasses distributed like cattle lymphomas. The lymph nodes were always affected,

and generally were involved in more than one site in a single animal. Liver, spleen, and kidneys were involved in 40% of the cases. The diaphragm was infiltrated in 3 animals, the subcutis of the skin in 2 (fig. 21), lungs in 2, the abomasum in 1, and peritoneum in 1. Heart, uterus, and thymus were not involved in any animals.

Microscopically, 10 ovine lymphomas were *lymphocytic* and 7 were *histiocytic*. The histomorphologic changes in affected organs resembled those in affected organs of cattle.

Malignant Lymphomas of Goats

The numbers of goats slaughtered for food is comparatively small, and annual rates vary compared to those of other animals; therefore, the annual rates of malignant lymphomas also vary (tables 1 and 3). Of the two histologically confirmed lymphomas of goats (table 2), one in a 4-year-old female slaughtered in poor condition had involvement of many skeletal and mesenteric lymph nodes. The other, in a 3-year-old female slaughtered in good condition, had involvement of all skeletal and visceral lymph nodes, heart, liver, and lungs.

Microscopically, the lymphoma of the former goat was of the *lymphocytic* type and that of the latter was of the *histiocytic* type. Histomorphologic changes observed in caprine lymphomas were similar to those of cattle.

Malignant Lymphomas of Horses and Mules

Many reports of malignant lymphomas in horses have appeared in the literature (28, 42, 43). Cornelius *et al.* (44) described in 1959 a plasma cell myelomatosis in a 16-year-old gelding (castrated male). The number of horses slaughtered for food in the United States has decreased gradually during the past 10 years (table 3). The apparent variations in rates of occurrence of malignant lymphoma in horses of our series (table 1) may be explained in part by irregular culling practices; slaughter populations are not uniform from year to year.

Two of the three histologically confirmed equine lymphomas (table 2) were in horses and one was in a mule. Both horses were aged. In one horse, all body lymph nodes were involved. In the other horse, only lumbar and sacral lymph nodes, muscles of the diaphragm, and extensor muscles of the rear legs were involved. The mule, aged and in poor condition, had cervical, mediastinal, and lumbar lymph nodes enlarged 20-25 times normal.

Microscopically, the lymphomas of both horses were classified as *histiocytic*; the lymphoma of the mule was *lymphocytic*.

THYMOMAS

Thymomas were observed in animals of all 5 species. In our experience they are relatively benign and are composed of cells of both reticular (epithelial) and lymphocytic types. Usually encapsulated, they do not ordinarily metastasize, though they may invade thoracic viscera.

In a few tumors one or the other of the two cell types may predominate, or the neoplasm may be composed entirely of cells of one type. When lymphocytic cells predominate, thymomas are sometimes difficult to distinguish from lymphomas of the thymus. Castleman (45) described criteria for diagnosis of thymoma. As already stated, thymomas are usually encapsulated and rarely metastasize, whereas malignant lymphomas usually involve other organs in addition to thymus. Sections should be taken from several sites of thoracic tumors suspected of being thymomas, because ratios of component cells can vary in different areas of a tumor.

Thymomas of Cattle

Jackson (46) described in detail 4 thymomas of cattle. Twenty-nine bovine thymomas were examined in our laboratory (table 2). Twenty-four of these occurred in cattle over 3 years old.

Grossly, the typical bovine thymoma was a nodular mass ranging from 10-20 cm in diameter. It was usually located in the anterior thorax (fig. 22). Some thymomas, however, were located in the lower neck anterior to the thoracic inlet. In one animal the neoplasm entered the thoracic inlet from the lower neck region. Most thymomas were encapsulated and lobulated. Color varied from grayish-white to yellow to light brown. Focal areas of hemorrhage and necrosis were occasionally observed on cut surfaces. The tumor was often attached to the lung, pericardium, or parietal pleura. Depending on the size and location of the neoplasm, varying degrees of interference with the functions of the structure of the anterior thorax and thoracic inlet may occur. Growth apparently progresses by expansion rather than by infiltration; metastases were observed in mediastinal lymph nodes of only one animal.

Microscopically, bovine thymomas typically had well-defined connective tissue capsules which in some areas were quite thick. Wide connective tissue septa extending inward from the capsule divided tumors into lobules of varying sizes. Frequently, neoplastic cells invaded the septa. Delicate stroma supported neoplastic cells. Hemorrhages, focal areas of necrosis, and infiltration by polymorphonuclear neutrophils were occasionally noted. Hassall's corpuscles or their degenerated forms were observed in 3% of tumors; this percentage would probably have been higher if serial sections had been examined. Two definite neoplastic cell types were recognized in bovine thymomas: *a*) a small, round cell morphologically resembling a lymphocyte and *b*) a larger cell with a vesicular oval nucleus, a prominent nucleolus, and relatively abundant

cytoplasm which resembled a reticulum cell. Probably both types of cells always occur in "typical" thymomas, but this is sometimes difficult to demonstrate if one type predominates.

In 20 bovine thymomas, the predominant cells were reticular cells, arranged in broad sheets. In these, small collections of lymphocytes were scattered throughout. Reticulum cells palisaded around small blood vessels in several cases (fig. 23). In the other 9 thymomas, lymphocytes predominated, with significantly fewer reticulum cells scattered throughout.

Thymomas of Pigs

Thymomas are rare in slaughtered pigs. All 5 histologically confirmed thymomas (table 2) occurred in 6-month-old pigs. All were located in the anterior thorax and measured 8-15 cm in diameter. They were grayish white with focal areas of necrosis. There were distinct capsules. No metastases were noted.

Microscopically, thymomas of pigs were similar to those of cattle. Reticulum cells predominated. Interestingly, "starry sky" effects (phagocytic macrophages) were observed in a few thymomas and were most numerous near areas of necrosis.

Thymomas of Sheep

Thymomas are apparently less common in sheep than in other animals. We found only 2 in our series (table 2). Both thymomas were located in the anterior thorax of adult female sheep. One, a firm encapsulated mass 12 cm in greatest dimension, was attached to the apical lobe of the right lung. The other, an encapsulated tumor, measured 30 cm and was not attached to other viscera. Neither metastasized. Microscopically, thymomas of sheep were similar to those of cattle. The predominant cell was the lymphocyte.

Thymomas of Goats

The rates of occurrence of thymomas in goats appear to be higher than those in other species of slaughter animals. During a short-term survey of neoplasms of goats in 1958 by the Federal Meat Inspection Service, 8 thymomas were discovered in approximately 100,000 slaughtered goats. Of 12 goats with histologically confirmed thymomas recorded during a 10-year period (table 2), 10 were 2-6 years old and 2 were 1 year old. All goats were in poor or fair condition before slaughter.

Grossly, the thymomas were large, tan, encapsulated masses located in the anterior thorax. They were firm and lobulated, ranging from 5-15 cm. One tumor weighed 8 pounds. Some tumors had focal areas of necrosis. Some were attached to lungs and had caused extensive subpleural atelectasis by their expansive growth. No tumors metastasized.

Microscopically, the thymomas were covered by thick, dense connective tissue capsules (fig. 24), and thick septa extended from capsules into the tumors. Morphologic characteristics of caprine thymomas were similar to those of bovine thymomas (fig. 25). Lymphocytes predominated in all tumors. Hassall's corpuscles were demonstrated in more than half the tumors.

Thymomas of Horses

Thymomas are apparently rare in horses. Both equine thymomas recorded in table 2 were in aged horses. One was a 15 cm encapsulated, cream-colored mass attached to the parietal pleura. The other was a 4 × 9 cm lobulated mass adjacent to the trachea in the lower neck. Neither tumor metastasized.

Microscopically, in both horses, reticulum cells predominated; small collections of lymphocytes were scattered throughout (fig. 26).

MASTOCYTOMAS

Mastocytomas are also called mast cell tumors, basophilic myelosarcomas, and mastosarcomas. Mastocytomas are composed of cells resembling and presumably derived from tissue mast cells. Cytoplasm characteristically contains prominent granules that stain metachromatically with certain aniline dyes. Although tissue mast cells have little morphologic resemblance to blood basophils, the biochemical components of the two cell types are similar, and the mastocytoma has also been called a basophilic myelosarcoma.

Mastocytomas were observed only in cattle and pigs of our series.

Mastocytomas of Cattle

In contrast to dogs, in which mastocytomas, particularly of the skin, occur frequently, cattle rarely have mastocytic neoplasms, according to a review by Groth *et al.* (47) who reported a mastocytoma in a bovine abomasum. Dodd (48) described a similar tumor in the tongue of a calf.

Mastocytomas are rare in slaughtered cattle. Only 12 bovine mastocytomas were confirmed in our laboratory (table 2). Ten cattle were adults; 2 were younger than 3 years.

Grossly, bovine mastocytomas were nodular masses ranging from 1-7.5 cm in greatest dimensions. They varied from white to yellow to green, depending on the amount of necrosis and number of polymorphonuclear eosinophils present. Some had foci of calcification. The mastocytomas were multiple in all cattle except one in which the mast cell infiltrates were in only one lymph node. Characteristically, bovine mastocytomas involve lymph nodes, skin, liver, spleen, lungs, skeletal muscles, heart, kidneys, omentum, pleura, pericardium, and peritoneum.

Microscopically, bovine mastocytomas were nonencapsulated, discrete nodular masses (fig. 27). Cells were clustered and were supported by delicate connective tissue stroma. In some tumors, they were separated into distinct lobules by prominent connective tissue septa. The neoplastic mast cells were similar to those of mastocytomas of other animals. Nuclei were eccentrically located, but occasionally they were centrally located. Coarse, discrete chromatin granules were prominent (fig. 28). A few nuclei were indented. Abundant eosinophilic cytoplasm and distinct cell walls were characteristic in fixed sections stained with hematoxylin and eosin. Staining with aniline dyes, such as Giemsa, revealed metachromatic cytoplasmic granules. Polymorphonuclear eosinophils observed in mastocytomas varied in number. Most eosinophils were found near blood vessels in connective tissue septa.

Mastocytomas of Pigs

Mastocytomas are relatively uncommon in pigs. Only 5 were observed in pigs of our series (table 2). All were located in dermis of the skin. Animals ranged in age from 6 months to 1½ years. The mastocytomas were nodular, measured 0.5–2.5 cm in diameter, and were a definite pink. They were observed in skin over entire carcasses. In fact, in one animal, they were even observed in the dermis of the head, ears, and feet. Mastocytomas are easily observed in slaughtered pigs because the epidermis is routinely removed in the dehairing process; they would be difficult to observe in intact animals. No metastatic lesions were observed in any carcasses.

Microscopically, the mastocytomas were discrete, circumscribed nodules located in the dermis. Cells were separated into nests of variable sizes by relatively thick connective tissue septa that branched into more delicate thin septa separating smaller groupings of cells (fig. 29). The large number of septa is characteristic of this neoplasm. As in mastocytomas of cattle, polymorphonuclear eosinophils in the tumors varied in amount from area to area but were concentrated mostly adjacent to septa. Neoplastic mast cells were round-to-polyhedral, with abundant cytoplasm and well-defined cell walls, and tended to be arranged in sheets. Nuclei were round and eccentrically located and contained distinct chromatin granules. Metachromatic granules were difficult to demonstrate.

Mastocytomas of Other Animals

Mastocytomas were not observed in sheep, goats, or horses.

GRANULOCYTIC SARCOMAS

Granulocytic sarcomas are also called malignant myeloma, myelosarcoma, chloroma, myelogenous leukemia, and myeloblastic sarcoma.

Granulocytic sarcomas were observed only in cattle and pigs (table 2). Typically, they are focal or diffuse proliferations of immature granulocytes (myelocytes or myeloblasts) and have granules that may be eosinophilic, neutrophilic, or basophilic.

Neoplasms composed of immature granulocytes are also called malignant myelomas or myelosarcomas because of the *myeloid* origin of neoplastic cells. In human hematopathology, the term "myeloma" is used to designate neoplasms composed of plasma cells, so-called "multiple myeloma." Immature granulocytes are quite different from plasma cells, and confusion of the names is unfortunate.

Granulocytic Sarcomas of Cattle

Granulocytic sarcomas are rare in cattle, and only a few have been reported in the literature (49, 50). Several examples were described in our earlier survey (12). All granulocytic sarcomas were composed of eosinophils; we did not see neutrophilic or basophilic types.

Two examples of granulocytic sarcomas of cattle examined in our laboratory are recorded in table 2. One was in a 20-month-old heifer and the other in a 6-year-old cow. Grossly, the outstanding characteristic was a green color observed in lymph nodes, liver, spleen, kidneys, lungs, and bone marrow. Affected organs were 2-3 times their normal size. The green color of gross organs was similar to that described in granulocytic sarcomas or chloromas of man (29).

Microscopically, neoplastic granulocytes formed discrete masses in distributions similar to those observed in some malignant lymphomas. Delicate stroma supported neoplastic granulocytes. Nuclei were round or ovoid and hyperchromatic and were located slightly eccentrically (fig. 30). Some nuclei were slightly indented. Cytoplasm contained numerous distinct eosinophilic granules. Most neoplastic granulocytes were similar to, but larger than, normal eosinophilic myelocytes or myeloblasts. Mature polymorphonuclear eosinophils were scarce.

In the liver, neoplastic granulocytes were observed in interlobular connective tissue and had formed wide collars around hepatic lobules, similar to infiltrates of some malignant lymphomas. Although hematologic information was not available, there was no evidence of leukemia; neoplastic granulocytes were not observed in sinusoids or blood vessels.

Eosinophilic granulocytic sarcomas must be distinguished from two non-neoplastic diseases of cattle in which a gross green color is associated with infiltrations of many mature eosinophils: *a) eosinophilic lymphadenitis*, in which the gross green color is associated with accumulations of mature eosinophilic leukocytes in sinuses of lymph nodes and *b) eosinophilic myositis* (51), in which appear massive accumulations of mature polymorphonuclear eosinophilic leukocytes in striated muscles.

Granulocytic Sarcomas of Pigs

Granulocytic sarcomas are apparently rare in pigs, as in cattle. Both histologically confirmed examples of granulocytic sarcomas in pigs of our series were in adult females (table 2). The color of the gross neoplasms was green like that of cattle. Visceral and skeletal lymph nodes, liver, heart, kidneys, bone, pancreas, and serous membranes were involved. In microscopic sections, infiltrates were composed of large cells resembling eosinophilic myeloblasts and myelocytes, except that they were larger (figs. 3 and 32). Few mature eosinophilic leukocytes were present.

Granulocytic Sarcomas of Other Animals

Granulocytic sarcomas were not observed in sheep, goats, or horses.

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FIGURE 1.—Malignant lymphoma (lymphocytic type), lymph node, bovine. *Note* uniformity of cells and scant amount of cytoplasm. Hematoxylin and eosin. Armed Forces Institute of Pathology (AFIP) negative 68-6492-1. $\times 500$

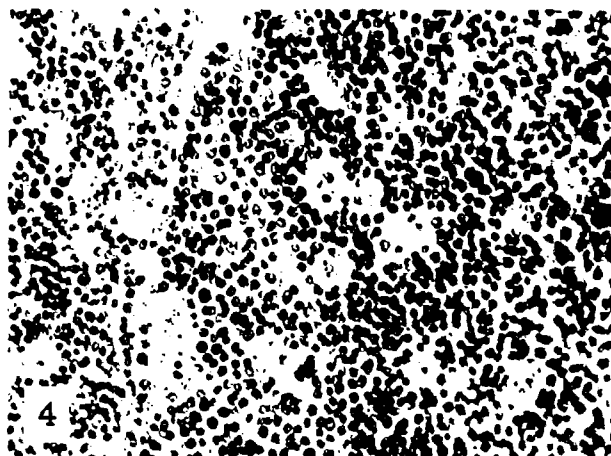
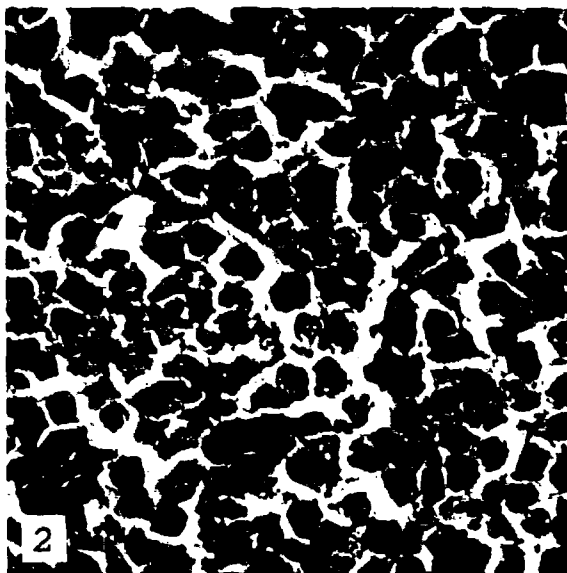
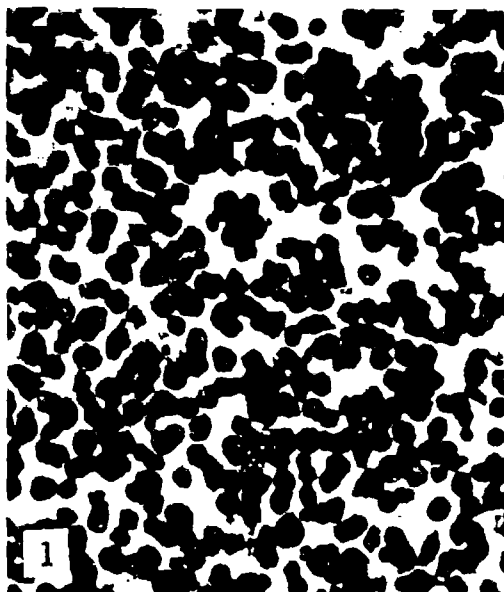
FIGURE 2.—Malignant lymphoma (histiocytic type), lymph node, bovine. Cells are large and have much cytoplasm and a vesicular nucleus containing a prominent nucleolus. Hematoxylin and eosin. AFIP negative 68-6492-2. $\times 600$

FIGURE 3.—Malignant lymphoma (histiocytic type), lymph node, goat. *Note* large vesicular indented nuclei with prominent nucleoli. Hematoxylin and eosin. AFIP negative 68-6492-3. $\times 500$

FIGURE 4.—Malignant lymphoma, lymph node, pig, showing "starry sky" effect. *Note* phagocytized nuclear debris. Hematoxylin and eosin. AFIP negative 68-6492-4. $\times 220$

FIGURE 5.—Malignant lymphoma, heart, bovine. *Note* multiple nodular growths at base of heart. AFIP negative 68-6492-5.

FIGURE 6.—Malignant lymphoma, heart, bovine, showing diffuse infiltration of neoplastic cells between muscle bundles and muscle fibers. Hematoxylin and eosin. AFIP negative 68-6492-6. $\times 40$



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FIGURE 7.—Malignant lymphoma, kidney, bovine, showing multiple nodular neoplastic masses. Armed Forces Institute of Pathology (AFIP) negative 68-6492-7.

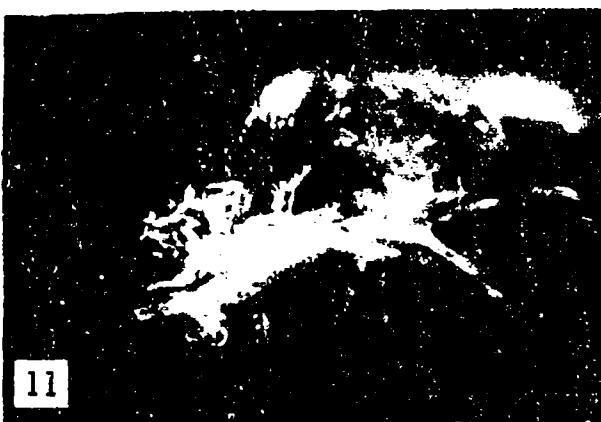
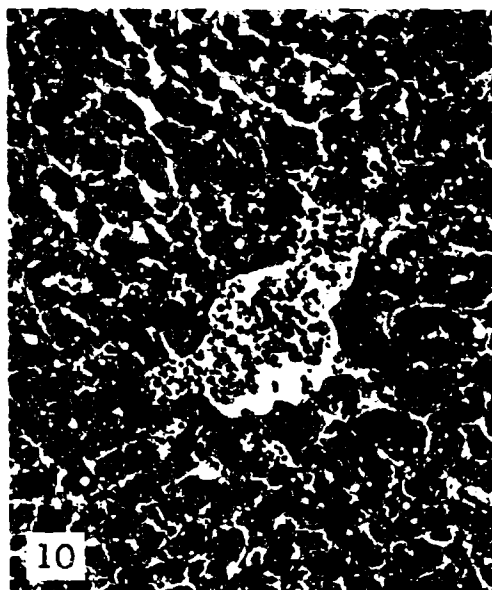
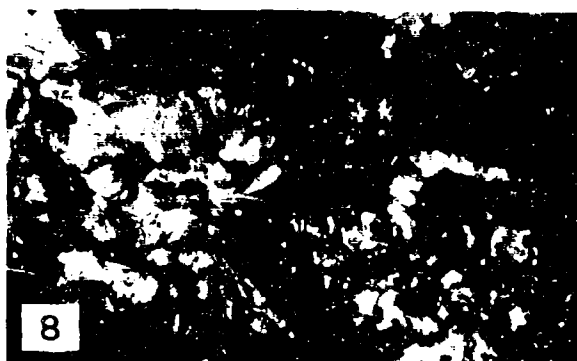
FIGURE 8.—Malignant lymphoma, uterus and cervix, bovine, showing multiple nodular growths on mucosal surface. AFIP negative 68-6492-8.

FIGURE 9.—Malignant lymphoma, uterus, bovine, showing infiltrations of neoplastic cells in endometrium and myometrium. Ductal structures in *center* of field are uterine glands. Hematoxylin and eosin. AFIP negative 68-6492-9. $\times 35$

FIGURE 10.—Malignant lymphoma, liver, bovine, showing neoplastic cells in sinusoids and central vein. Hematoxylin and eosin. AFIP negative 68-6492-10. $\times 150$

FIGURE 11.—Spinal meninges, bovine, showing nodular growths of malignant lymphoma. AFIP negative 68-6492-11.

FIGURE 12.—Malignant lymphoma, liver, pig, showing multiple nodular growths. AFIP negative 68-6492-12.



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FIGURE 13.—Malignant lymphoma, liver, pig, showing extensive infiltration of neoplastic cells which have almost completely replaced cells of liver cords. Hematoxylin and eosin. Armed Forces Institute of Pathology (AFIP) negative 68-6492-13. $\times 70$

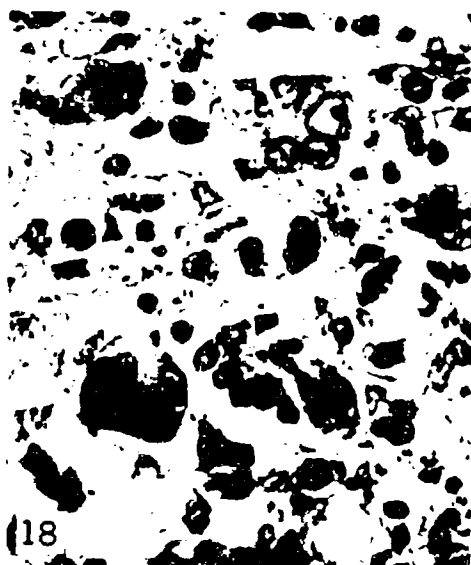
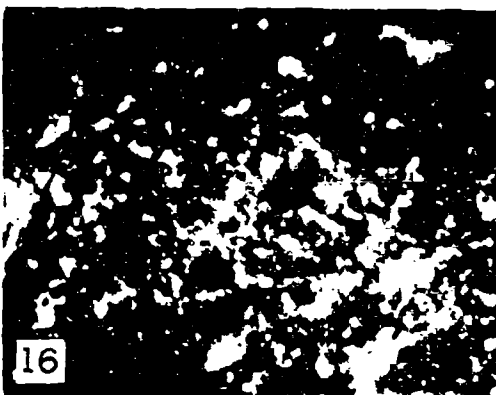
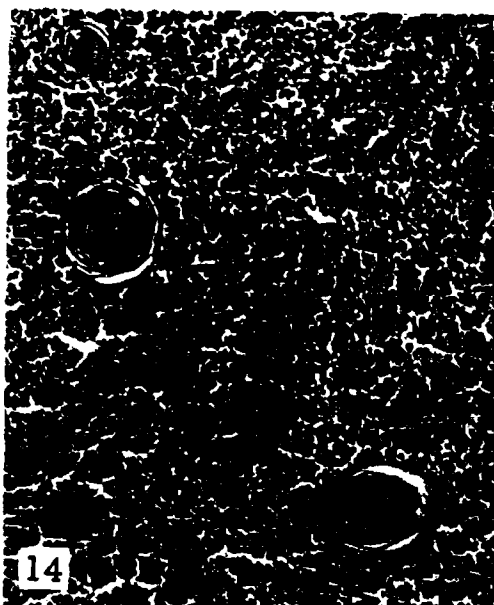
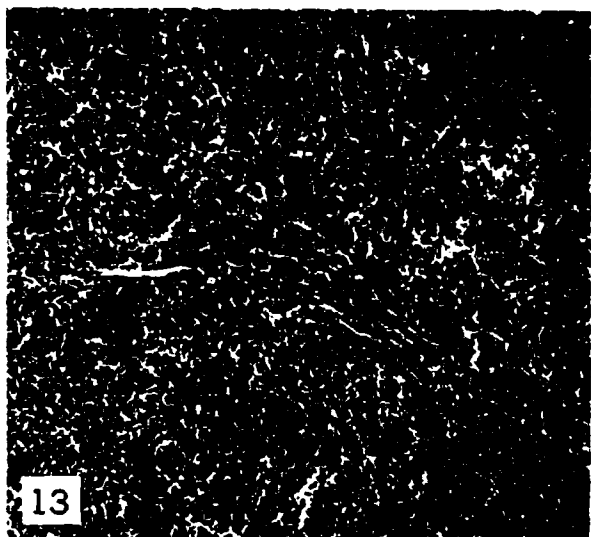
FIGURE 14.—Malignant lymphoma, thymus, pig, showing infiltration by neoplastic cells. Large concentric structures are remaining Hassall's corpuscles. Hematoxylin and eosin. AFIP negative 68-6492-14. $\times 130$

FIGURE 15.—Chronic granulomatous disease, spleen, pig, showing enlarged spleen. For comparison, normal spleen is shown (*nearest ruler*). AFIP negative 68-6492-15.

FIGURE 16.—Close-up view of whitish-gray mottled spleen of pig with chronic granulomatous disease. AFIP negative 68-6492-16.

FIGURE 17.—Chronic granulomatous disease, spleen, pig. *Note* extensive fibrosis and scarring of white pulp. Hematoxylin and eosin. AFIP negative 68-6492-17. $\times 35$

FIGURE 18.—Chronic granulomatous disease, spleen, pig, showing giant cells. Hematoxylin and eosin. AFIP negative 68-6492-18. $\times 500$



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FIGURE 19.—Chronic granulomatous disease, liver, pig. *Note* large amount of interlobular connective tissue containing small, diffuse collections of leukocytes. Hematoxylin and eosin. Armed Forces Institute of Pathology (AFIP) negative 68-6492-19. $\times 35$

FIGURE 20.—Chronic granulomatous disease, lymph node, pig, showing extensive fibrosis of germinal centers. Hematoxylin and eosin. AFIP negatives 68-6492-20. $\times 115$

FIGURE 21.—Malignant lymphoma, subcutaneous tissue, sheep. *Note* tumor cells invading dermis. Lymph nodes are also affected. Hematoxylin and eosin. AFIP negative 68-6492-21. $\times 70$

FIGURE 22.—Thymoma, bovine, showing encapsulation and lobulation. AFIP negative 68-6492-22.

FIGURE 23.—Thymoma, bovine. *Note* presence of many reticulum cells with fewer smaller, dark-staining lymphocytes. Reticulum cells palisade around a small blood vessel. Hematoxylin and eosin. AFIP negative 68-6492-23. $\times 400$

FIGURE 24.—Thymoma, goat. *Note* thick capsule and septa. Marked differences in staining quality of neoplastic cells are seen at this magnification. Hematoxylin and eosin. AFIP negative 68-6492-24. $\times 115$

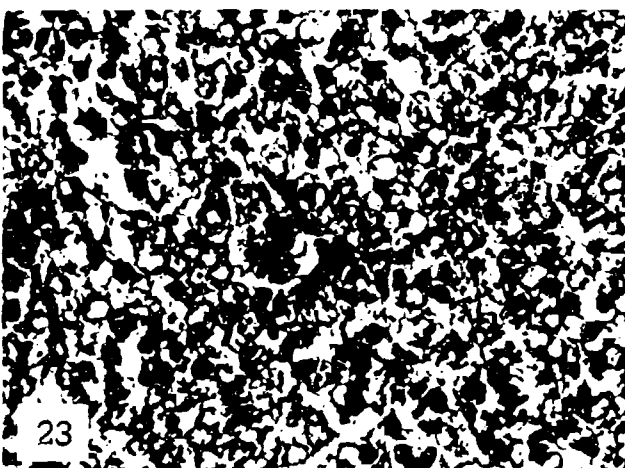
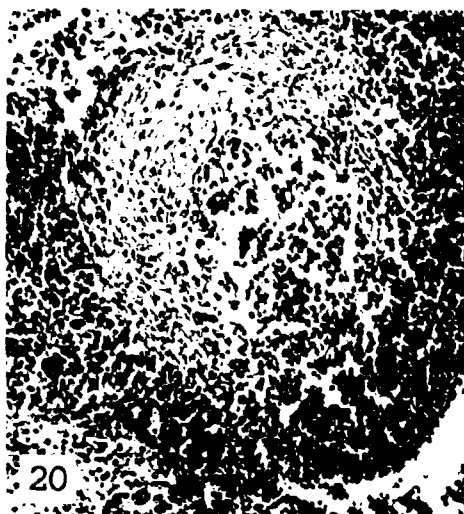


FIGURE 25.—Thymoma, goat. Note lobule formation by thick connective tissue septa. Hematoxylin and eosin. Armed Forces Institute of Pathology (AFIP) negative 68-6492-25. $\times 80$

FIGURE 26.—Thymoma, horse, showing two cell types. Larger, light-staining cells are reticulum cells, and dark-staining cells are lymphocytes. Hematoxylin and eosin. AFIP negative 68-6492-26. $\times 500$

FIGURE 27.—Mastocytoma, liver, bovine, showing nodular appearance. Growth occurs by expansion rather than infiltration. Hematoxylin and eosin. AFIP negative 68-6492-27. $\times 100$

FIGURE 28.—Mastocytoma, lung, bovine. Note neoplastic cells lining thin connective tissue septa. Dark-staining cytoplasmic granules are in these cells. Smaller cells are polymorphonuclear eosinophils. Giemsa. AFIP negative 68-6492-28. $\times 600$

FIGURE 29.—Mastocytoma, dermis of skin, pig. Neoplastic cells are separated into lobules by connective tissue septa. Glandular structures beneath the neoplasm are sweat glands. Hematoxylin and eosin. AFIP negative 68-6492-29. $\times 40$

FIGURE 30.—Granulocytic sarcoma (malignant myeloma), liver, bovine. Dark-staining ovoid nuclei are eccentrically located, and a moderate amount of cytoplasm can be seen. Note delicate stromal tissue supporting neoplastic cells. Giemsa-stained sections showing eosinophilic granules in cytoplasm. AFIP negative 68-6492-30. $\times 530$

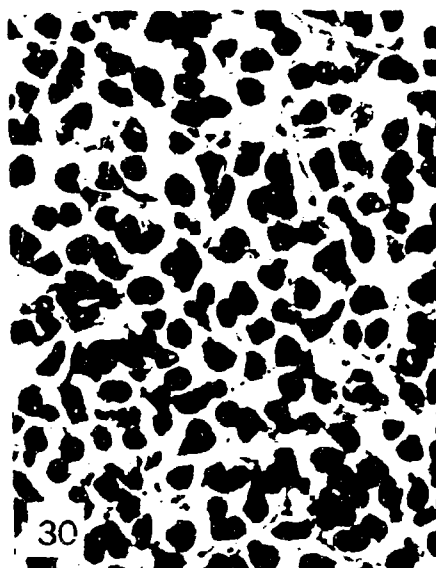
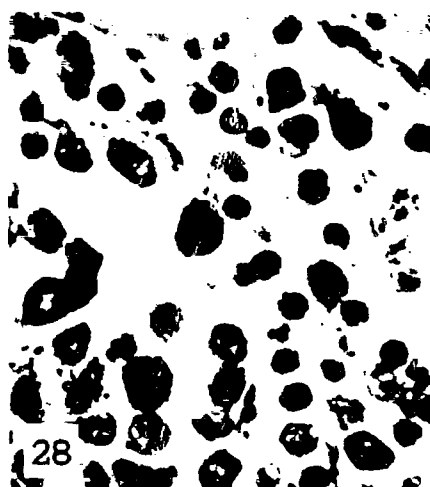
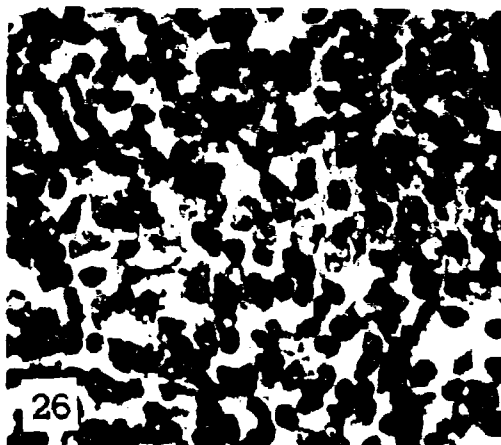
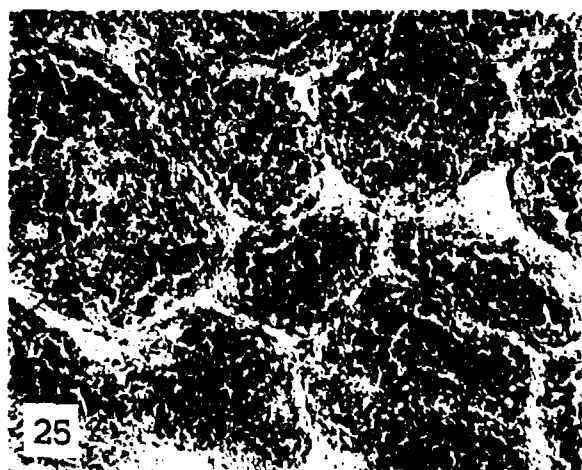


FIGURE 31.—Granulocytic sarcoma, lymph node, pig. *Note* diffuse infiltration of neoplastic granulocytes, leaving a small lymphoid focus and a fragment of trabeculum. Hematoxylin and eosin. Armed Forces Institute of Pathology (AFIP) negative 68-6492-31. $\times 80$

FIGURE 32.—Higher magnification of figure 31, showing details of neoplastic granulocytes and delicate supporting stroma. Giemsa-stained slides showing eosinophilic cytoplasmic granules. AFIP negative 68-6492-32. $\times 600$

